

**REMARKS****Status of the Claims**

Claims 32 and 35 has been amended to recite intradermally or subcutaneously administering (or delivering) total tumor cell RNA to cutaneous cells. Support for this amendment can be found, for example, on page 5, lines 19-26, and in Examples 2 and 3 (pages 26 and 27) of the application. Claim 35 also now recites, wherein the total tumor cell RNA is taken from an autologous tumor associated with the cancer. Claims 37-42 have been canceled without prejudice or disclaimer.<sup>1</sup> Claim 43 has been amended to recite administering RNA which comprises antigen RNA, and to specify that the antigen is an allogenic transplant tissue antigen.<sup>2</sup> Claims 50-53 have been added. Support for these claims can be found, for example, on page 21, lines 22-25 of the application.

Claims 32-36 and 43-46 and 50-53 are pending and at issue.

**Claim Objections**

The Examiner has objected to claims 44 and 45 as being in improper dependent form. The Examiner alleges that claims 44 and 45, which respectively recite cellular RNA and cellular mRNA, are broader than claim 43, which previously recited antigen RNA. Claim 43 has been amended to recite "RNA which comprises antigen RNA". Applicant respectfully submits that claims 44 and 45 are in proper dependent form.

**Claim Rejections - 35 U.S.C. § 112, first paragraph**

Claims 32-36 stand rejected as not enabled by the specification. The Examiner admits that the specification is enabling for inducing an immune response to a tumor in a subject by

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<sup>1</sup> Applicant respectfully submits, however, that claims 37-42 are patentable, and reserves the right to prosecute these claims in a continuation application.

<sup>2</sup> Applicant also respectfully submits that claim 43 is patentable when the antigen is an autoantigen, or allergen, and reserves the right to prosecute claims directed to this subject matter in a continuation application.





There is no motivation to combine Qiu and Nair, and even if combined, there is no reasonable expectation of success. The primary reference, Qiu, does not disclose or suggest administration of fractionated tumor cell RNA *or* total tumor cell RNA. There is no motivation to consult Nair, which suggest the interchangeability of the two, when the use of tumor cell RNA is not taught or suggested in Qiu.

Nevertheless the Examiner concludes, presumably based on the teaching of the present application, that it would have been obvious to substitute the antigens in Qui with total tumor cell RNA. Even if this were the case, there is no reasonable expectation of success upon making this purportedly obvious substitution. Qui and Nair disclose different routes of administration, i.e., Qui discloses particle bombardment of the epidermis and liver, whereas Nair exclusively teaches intraperitoneal vaccination or vaccination via infusion. In Nair, a purified population of blood or lymphoid derived dendritic cells were pulsed *ex vivo*, as opposed to an *in vivo* heterogenous population of epidermal cells. Neither reference discloses or suggests that an immune response to a tumor can be induced by intradermally or subcutaneously administering total tumor cell RNA to epidermal cells.

Segal seeks to provide compositions and methods for improved vaccines by improving the uptake of antigens by antigen presenting cells upon introduction of opsonin-enhanced cells which comprises the selected antigen. Fibrosarcoma cells are one of the antigens mentioned in Segal. Segal does not, however, disclose or suggest that an immune response to a tumor can be induced by intradermally or subcutaneously administering total tumor cell RNA to epidermal cells, or provide motivation to combine Qui and Nair.

Applicant respectfully requests that the obviousness rejection of claims 32 and 33 be withdrawn.

Claims 37-42 have been rejected as obvious over Ashley (J. Exp. Med. 186:1177-82) in view of Beissert (J. Immunol. 154:1280-86). These claims have been canceled without prejudice, rendering this rejection moot.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

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Respectfully submitted,

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